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EXAMINER	
CLARK, AMY LYNN	
ART UNIT	**PAPER NUMBER**
1655	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,725	OMORI ET AL.	
	Examiner	Art Unit	
	Amy L. Clark	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *8-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendment filed on 31 October 2006 with the amendment of claims 1, 2, 4 and 6.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-7 are under examination.

Election/Restrictions

This application contains claims 8-26, which are drawn to an invention nonelected without traverse in "Response to Election / Restriction Filed" filed on 12 May 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Newly applied as necessitated by amendment.

Enablement is considered in view of the *Wands* factors (MPEP 2164.O1(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: The claims are drawn to any composition comprising any type of unadsorbed fraction obtained by any solvent system, wherein said unabsorbed fraction is formed by subjecting a barley shochu stillage: obtained by the production of shochu from a barley as a raw material: to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent, where unabsorbed product of said separation treatment is said unabsorbed fraction, in which wherein the unadsorbed fraction contains plural peptides having an average chain length of from 3.0 to 5.0, and these peptides comprise from 24 to 38 % by weight of glutamic acid, from 4 to 20 % by weight of glycine, from 5 to 10% by weight of aspartic acid, from 4 to 9% by weight of proline and from 4 to 8% by weight of serine on the basis of the total weight of the amino acids forming said peptides, and wherein said compound is capable of inhibiting the onset of alcoholic hepatopathy and/or capable of healing alcoholic hepatopathy.

Breadth of the Claims: The claims are broad in that a therapeutically effective amount of any composition comprising any type of unadsorbed fraction, wherein said unabsorbed fraction is formed by subjecting a barley shochu stillage: obtained by the

production of shochu from a barley as a raw material: to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent, where unabsorbed product of said separation treatment is said unabsorbed fraction, in which wherein the unadsorbed fraction contains plural peptides having an average chain length of from 3.0 to 5.0, and these peptides comprise from 24 to 38 % by weight of glutamic acid, from 4 to 20 % by weight of glycine, from 5 to 10% by weight of aspartic acid, from 4 to 9% by weight of proline and from 4 to 8% by weight of serine on the basis of the total weight of the amino acids forming said peptides, may be administered to inhibit the onset of any type of alcoholic hepatopathy and/or heal any type of alcoholic hepatopathy in a patient. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

Guidance of the Specification and Existence of Working Examples: The specification describes a composition comprising an unadsorbed fraction, wherein said unabsorbed fraction is formed by subjecting a barley shochu stillage: obtained by the production of shochu from a barley as a raw material: to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent, where unabsorbed product of said separation treatment is said unabsorbed fraction, in which wherein the unadsorbed fraction contains plural peptides having an average chain length of from 3.0 to 5.0, and these peptides comprise from 24 to 38 % by weight of glutamic acid, from 4 to 20 % by weight of glycine, from 5 to 10% by weight of aspartic acid, from 4 to 9% by weight of proline and

from 4 to 8% by weight of serine on the basis of the total weight of the amino acids forming said peptides (See pages 10 and 11). The specification further describes a method of determining the effect of feeding freeze-dried powder of liquid fraction (A) of barley shochu stillage on rats (See "Experiment 1", pages 12-16), wherein the specification concludes that the foregoing results have revealed that the freeze-dried powder (A') of the liquid fraction (A) of the barley shochu stillage is not suggestive of the actual use as a drug for positively inhibiting the onset of alcoholic hepatopathy. The specification further describes a method of determining the effect of feeding a desorbed fraction obtained by subjecting the liquid fraction of the barley shochu fraction to a separation treatment by adsorption using a synthetic adsorbant and eluting the resulting adsorbed fraction with an alkali on rats (See "Experiment 2", pages 16-19), wherein the specification concludes that the foregoing results have revealed that the freeze-dried powder (B') of the desorbed fraction (B) of the barley shochu stillage has slightly shown a tendency of inhibiting induction of the alcoholic hyerlipemia, but not shown a tendency of inhibiting induction of the alcoholic fatty liver and alcoholic hepatitis and that the desorbed fraction is substantially free from the activity of inhibiting the onset of alcoholic hepatopathy. The specification further describes a method of determining the effect of feeding a fraction formed by subjecting the liquid fraction of the barley shochu stillage to a separation treatment by adsorption using a synthetic adsorbant (C) on rats (See "Experiment 3", pages 19-22), wherein the specification concludes that the freeze-dried powder (C') of the unadsorbed fraction (C) has the marked activity of inhibiting the onset of alcoholic hepatopathy. The specification further describes other methods involving

various fractions of barley shochu stillage, wherein the various fractions are tested on rats, which have inconclusive results with respect to the inhibition of alcoholic hepatopathy (See "Experiment 5" and "Experiment 6" (pages 23-33). Nowhere in the specification are *in vitro* or *in vivo* examples provided that show healing of alcoholic hepatopathy.

The specification envisions that any composition comprising any type of unadsorbed fraction obtained by any solvent system, wherein said unabsorbed fraction is formed by subjecting a barley shochu stillage: obtained by the production of shochu from a barley as a raw material: to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent, where unabsorbed product of said separation treatment is said unabsorbed fraction, in which wherein the unadsorbed fraction contains plural peptides having an average chain length of from 3.0 to 5.0, and these peptides comprise from 24 to 38 % by weight of glutamic acid, from 4 to 20 % by weight of glycine, from 5 to 10% by weight of aspartic acid, from 4 to 9% by weight of proline and from 4 to 8% by weight of serine on the basis of the total weight of the amino acids forming said peptides will have utility in humans in inhibiting the onset of any type of alcoholic hepatopathy and/or healing any type of alcoholic hepatopathy.

However, no working examples are provided with regard to a method for inhibiting the onset of all types of alcoholic hepatopathy nor are any working examples provided with regard to a method of healing any or all types of alcoholic hepatopathy. Furthermore, no working examples are provided that demonstrate the efficacy of any

composition comprising any type of unadsorbed fraction obtained by any solvent system, wherein said unabsorbed fraction is formed by subjecting a barley shochu stillage: obtained by the production of shochu from a barley as a raw material: to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent, where unabsorbed product of said separation treatment is said unabsorbed fraction, in which wherein the unadsorbed fraction contains plural peptides having an average chain length of from 3.0 to 5.0, and these peptides comprise from 24 to 38 % by weight of glutamic acid, from 4 to 20 % by weight of glycine, from 5 to 10% by weight of aspartic acid, from 4 to 9% by weight of proline and from 4 to 8% by weight of serine on the basis of the total weight of the amino acids forming said peptides in the inhibiting the onset of any type of alcoholic hepatopathy and/or healing any type of alcoholic hepatopathy.

Predictability and State of the Art: The state of the art at the time the invention was made was unpredictable and underdeveloped. For example, Blair et al. (Reference U) teaches that mortality in chicks from fatty liver and kidney syndrome was not significantly influenced by cereal type, such as barley. Please note that the ability of animal models to mirror conditions in humans is limited. For example, Ponnappa (Reference V, page 102, "Conclusions") teaches that many alcohol-induced conditions in humans are irreversible and researchers have been unable to produce such irreversible organ damage in animal models. Ponnappa further teaches that one reason for this inability may be that such alcohol-related disorders in humans take many years

of alcohol consumption to develop in humans and that differences among species may exist in disease pathogenesis.

Thus, while the claim-designated method may be useful for providing such an effect, Applicant does not disclose a method comprising the administration of any composition comprising any type of unadsorbed fraction obtained by any solvent system, wherein said unabsorbed fraction is formed by subjecting a barley shochu stillage: obtained by the production of shochu from a barley as a raw material: to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent, where unabsorbed product of said separation treatment is said unabsorbed fraction, in which wherein the unadsorbed fraction contains plural peptides having an average chain length of from 3.0 to 5.0, and these peptides comprise from 24 to 38 % by weight of glutamic acid, from 4 to 20 % by weight of glycine, from 5 to 10% by weight of aspartic acid, from 4 to 9% by weight of proline and from 4 to 8% by weight of serine on the basis of the total weight of the amino acids forming said peptides will have utility in humans in inhibiting the onset of any type of alcoholic hepatopathy and/or healing any type of alcoholic hepatopathy.

The Office further notes that while the specification discloses that the claim designated composition will have utility in humans in inhibiting the onset of any type of alcoholic hepatopathy and/or healing any type of alcoholic hepatopathy, nowhere in the specification or in the limitations does Applicant direct the claimed subject matter to the administration of that any composition comprising all types of unadsorbed fraction obtained by any solvent system, wherein said unabsorbed fraction is formed by

subjecting a barley shochu stillage: obtained by the production of shochu from a barley as a raw material: to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent, where unabsorbed product of said separation treatment is said unabsorbed fraction, in which wherein the unadsorbed fraction contains plural peptides having an average chain length of from 3.0 to 5.0, and these peptides comprise from 24 to 38 % by weight of glutamic acid, from 4 to 20 % by weight of glycine, from 5 to 10% by weight of aspartic acid, from 4 to 9% by weight of proline and from 4 to 8% by weight of serine on the basis of the total weight of the amino acids forming said peptides to any subject.

It should be noted that at the time of filing of the present application, the art of medicine did not recognize the administration of any composition comprising all types of unadsorbed fraction obtained by any solvent system, wherein said unabsorbed fraction is formed by subjecting a barley shochu stillage: obtained by the production of shochu from a barley as a raw material: to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent, where unabsorbed product of said separation treatment is said unabsorbed fraction, in which wherein the unadsorbed fraction contains plural peptides having an average chain length of from 3.0 to 5.0, and these peptides comprise from 24 to 38 % by weight of glutamic acid, from 4 to 20 % by weight of glycine, from 5 to 10% by weight of aspartic acid, from 4 to 9% by weight of proline and from 4 to 8% by weight of serine on the basis of the total weight of the amino acids forming said peptides to inhibit the onset of any type of alcoholic hepatopathy and/or heal any type of alcoholic

hepatopathy in humans.

Amount of Experimentation Necessary: The quantity of experimentation necessary to carry out the claimed invention is high, as the skilled artisan could not rely on the prior art or instant specification to teach how to make and use any any composition comprising all types of unadsorbed fraction obtained by any solvent system, wherein said unabsorbed fraction is formed by subjecting a barley shochu stillage: obtained by the production of shochu from a barley as a raw material: to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent, where unabsorbed product of said separation treatment is said unabsorbed fraction, in which wherein the unadsorbed fraction contains plural peptides having an average chain length of from 3.0 to 5.0, and these peptides comprise from 24 to 38 % by weight of glutamic acid, from 4 to 20 % by weight of glycine, from 5 to 10% by weight of aspartic acid, from 4 to 9% by weight of proline and from 4 to 8% by weight of serine on the basis of the total weight of the amino acids forming said peptides in the inhibition of the onset of any type of alcoholic hepatopathy and/or the healing of any type of alcoholic hepatopathy in humans. In order to carry out the claimed invention, one of ordinary skill in the art would have to identify compositions comprising all types of unadsorbed fraction obtained by any solvent system, wherein said unabsorbed fraction is formed by subjecting a barley shochu stillage: obtained by the production of shochu from a barley as a raw material: to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent,

where unabsorbed product of said separation treatment is said unabsorbed fraction, in which wherein the unadsorbed fraction contains plural peptides having an average chain length of from 3.0 to 5.0, and these peptides comprise from 24 to 38 % by weight of glutamic acid, from 4 to 20 % by weight of glycine, from 5 to 10% by weight of aspartic acid, from 4 to 9% by weight of proline and from 4 to 8% by weight of serine on the basis of the total weight of the amino acids forming said peptides that can be administered in a therapeutically effective dose with an acceptable level of side-effects.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, Claims 1-7 are not considered to be fully enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "a barley" in line 6, "the amino acids" in lines 14 and 15, and "said compound" in line 16. There is insufficient antecedent basis for these limitations in the claim.

Response to Arguments

Claim Rejections - 35 USC § 112

Newly amended claims 1, 2, 4 and 6 and claims 3, 5 and 7 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of Claims 1-7 are uncertain because it is unclear as to the identification of the ingredients to which Applicant intends to direct the subject matter. Although the use of common names or traditional/ethanopharmacological names is permissible in patent applications, the standard Latin genus-species name of each ingredient should accompany non-technical nomenclature as a means for identifying the subject botanical as noted in this application. The common name or traditional/ethanopharmacological name may have several different Latin names referring to various genus-species of the plant and it is unclear as to which genus and species Applicant is referring. The lack of clarity renders the claims indefinite since the resulting claims do not clearly set forth the metes and bounds of the patent protection desired. Applicant may overcome the rejection by placing the genus-species name of "barley" in parentheses after the term "barley".

This rejection is maintained for reasons of record set forth in the paper mailed on 31 May 2006 and repeated below, slightly altered to take into consideration Applicant's amendment filed on 31 October 2006.

Applicant's arguments have been thoroughly considered, but the rejection remains the same for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant argues that the term "barley" is well known in the art and that the following is submitted for the understanding of the Examiner. Applicant further argues that, usually, two-rowed barley is used for production of distilled spirit (shochu) and, in general, various kinds of barley are classified into the following categories, Six-rowed barley --- Hulled barley (small barley), Naked barley and Two-rowed barley --- Malting barley, Food barley (large barley). Applicant further argues that other than the above classification, they are alternatively classified into glutinous barley and non-glutinous barley. Applicant further argues that two-rowed barley was introduced from Europe as a raw material for beer in the early Meiji era, which marked the start of two-rowed barley cultivation in Japan. Applicant further argues that because of various requirements to be qualified as a beer material, including a large grain size, the high content of extractive components for beer, and a relatively small variation in raw grains, six-rowed barley was not much favored among beer brewers due to its small grain size and a relatively large variation in grains, making two-rowed barley a more preferable choice for beer brewing. Applicant further argues that this is the reason why two-rowed barley has been named as malting barley, that there is no such a plant called as "malting barley" (biru-mugi), and its botanical name is barley (oomugi). Applicant further argues, that to be exact, malting barley is beer barley (biru-oomugi), or two-rowed barley for beer brewing, that is, a kind of name equivalent to noodle wheat and/or bread wheat

and that ground (Milled) large-grain barley having less loss, that is, two-rowed barley, is used among various types of barley as a material for distilled spirit. Applicant further argues that food barley includes such a kind of barley as well as other edible barley. Applicant further argues that two-rowed barley is characterized in its larger grain size in comparison with six-rowed barley, popularly used for barley tea and the like and that the hull (so-called bran portion) of barley contains fat, proteins, and insoluble fibers, etc. Applicant further argues that if the whole grain of barley (husked barley) is used for brewing, the quality of the resulting liquor will be poor and for this reason, approximately 35% of grain closer to its outer skin is removed for brewing purposes (this process is referred to as "65% polishing"). Applicant further argues that the skin portion of barley is removed for brewing, two-rowed barley, which has a relatively large grain size, is suitable. Applicant further argues process of beer brewing, a malt-derived diastatic enzyme is used in order to saccharize starch contained in the material. In contrast, in a brewing process of distilled spirit, Aspergillus oryzae (koji-kin), which is a kind of fungus, is grown on the material; and subsequently, a diastatic enzyme produced by the koji-kin saccharizes the starch and that this process is called as koji production (seikou). Applicant further argues that two-rowed barley, which has a relatively large grain size, has another advantage in its easier manipulation in the process of koji production and two-rowed barley is the barley used for production of distilled spirit.

However, this is not found persuasive because, as Applicant points out, there are several different types (species) of barley and due to the fact that there are many different types of barley, these claims are ambiguous. Applicant is directed to the

reference, http://www.ibiblio.org/pfaf/cgi-bin/find_lat?LAT=&COM=barley&FAM=&RATING=1 (Reference W), wherein http://www.ibiblio.org/pfaf/cgi-bin/find_lat?LAT=&COM=barley&FAM=&RATING=1 teaches that there are several species of barley and that "common barley" has several species names referring to different species. Although the Examiner appreciates Applicant's description of the various types of barley, Applicant is reminded that the claims simply recite the general term "a barley" and do not provide an adequate description of the exact genus to which Applicant is referring. Please note that the features upon which applicant relies (i.e., the specific type of barley used in Applicant's claimed invention) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, although Applicant believes that only one type of barley may be used in this particular process, Applicant has not provided adequate evidence to show that no other types of barley may be used in the instantly claimed invention and Applicant has most certainly not described, in the claims as written, a specific type of barley used in the instantly claimed invention. It appears from Applicant's description of the process, which is found in Applicant's argument above and not in the claims themselves, that Applicant assumes that one of ordinary skill in the art would only perform this particular process of production in Japan, however, this limitation is not inserted in the claims, nor is this an accurate assumption. Therefore, the rejection is maintained.

Claim Rejections - 35 USC § 102

Newly amended claims 1, 2 and 4 are and claim 3 remains rejected under 35 U.S.C. 102(a) as being anticipated by Omori et al. (N*).

Omori teaches a composition having a fatty liver suppressing activity fractionated from residual liquid of barley *shochu* liquor distillation comprising of an unadsorbed fraction obtained by subjecting barley *shochu* stillage by-produced in the production of barley *shochu* to solid-liquid separation and filtering the material to provide a liquid fraction (See abstract and paragraph 0014 on page 5), please note that the liquid fraction reads on a composition. Omori does not expressly teach an unadsorbed fraction formed by subjecting barley *shochu* stillage to solid-liquid filtration, wherein the unadsorbed fraction contains peptides with an average chain length of 3 to 5 and wherein the peptides comprise 24 to 38% glutamic acid, 4 to 20% glycine, 5 to 10% aspartic acid, 4 to 9% proline and 4 to 8% serine, nor does Omori teach that the total content of amino acids derived from the peptides is from 8 to 14% by weight, nor does Omori teach that the fraction further contains free amino acids, free saccharides, polysaccharides and organic acids nor does Omori teach the fraction contains from 4 to 12% by weight of the free amino acids, from 5 to 10% by weight of the free saccharides, from 15 to 25% by weight of the polysaccharides and from 2 to 8% by weight of the organic acids. However, the composition and fraction, as taught by Omori, is obtained in the same way and produced in the same manner as the composition and fraction claimed by Applicant and is one and the same as the composition and fraction claimed by Applicant. Therefore, the peptide length, amount of amino acids in the peptides,

amount of amino acids derived from the peptides and the amount of saccharides, polysaccharides and organic acids in the composition taught by Omori are the same as that claimed by Applicant because these components are inherent to the composition taught by Omori and claimed by Applicant, absent evidence to the contrary.

Therefore, the reference anticipates the claimed subject matter.

This rejection is maintained for reasons of record set forth in the paper mailed on 31 May 2006 and repeated below, slightly altered to take into consideration Applicant's amendment filed on 31 October 2006.

Applicant's arguments have been thoroughly considered, but the rejection remains the same for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant argues that the composition according to the present invention is produced by obtaining "an unadsorbed fraction obtained by subjecting a barley shochu stillage obtained as the by-product in the production of shochu from barley to solid/liquid separation and then subjecting the liquid fraction thus obtained to a separation treatment by adsorption", whereas, in contrast, the composition according to Omori is produced as follows; a liquid fraction is obtained by subjecting a barley shochu stillage (residual liquid), which is obtained as the by-product in the process of producing shochu (distilled spirit) from barley, to solid/liquid separation; and then, the liquid fraction thus obtained is subjected to alkali addition treatment to obtain an alkali soluble fraction; the alkali soluble fraction thus obtained is then neutralized with an acid to obtain a neutral soluble fraction; and finally, a precipitated fraction is obtained after addition of ethanol to

the neutral soluble fraction." Applicant further argues that there are fundamental differences in production process between the composition according to the present invention and the resulting composition according to Omori (see also the drawings of Omori). Applicant further argues that a difference between the two compositions is percent composition and that the composition according to the present invention contains the following elements (see, for example, Applicants' claim 4): Organic Acid 2-8%, Polysaccharide 15-25%, Free Amino Acid 4-12%, Free Sugar 5-10%. The composition according to Omori contains the following elements: Organic Acid 32-38%, Protein 28-34% and Hemicellulose 25-31%. Applicant further argues that the compositions made by the processes of the cited art are completely different from the composition of the present invention, for example, there is no overlap in organic acid concentration. Applicant further argues that as set forth in further detail in Applicants' specification, one of ordinary skill in the art would not have expected the unexpected effects produced by a composition according to the present invention, that is that the inhibition of the onset of alcoholic liver injury is unexpected based on the known activity of inhibiting the onset of orotic acid-induced hepatopathy disclosed by Omori or based on the known activity of inhibiting the onset of D-galactosamine-induced hepatopathy disclosed by other publicly known documents. Applicant further argues that Omori describes that a composition comprising an ethanol-insoluble fraction containing an organic acid, protein and hemicellulose and formed by subjecting a barley shochu stillage to solid-liquid separation to obtain a liquid fraction, adding an alkali to the liquid fraction to collect with ethanol to accelerate synthesis of fatty acid or neutral fat in the

liver, inhibiting decomposition of fatty acid in the liver and the like. Applicant further argues that the alcoholic hepatitis is known to be hepatitis which is induced such that acetaldehyde or acetic acid, a metabolite of ethanol or active oxygen generated in producing the same damages hepatocytes. Applicant further argues that the alcoholic hyperlipemia is known to be triggered such that excess neutral fat accumulated in the liver is released to blood in large quantities as a secretory very low density lipoprotein (VLDL). Applicant further argues that such an alcoholic hepatopathy, it is known that lesion of hepatitis, such as balloon-like swelling or necrosis of hepatocytes, or a fatty liver comprising hepatocytes containing large fatty drops is progressed mainly on the terminal hepatic vein peripheral region of the hepatic lobule. Applicant further argues that incidentally, the liver is an assembly of a large number of the hepatic lobules each having a diameter of 1 mm in which the hepatic lobule partitioned by an interlobular connective tissue functions as one unit. Applicant further argues that accordingly, in view of the causative sequence of such hepatopathies, the alcoholic hepatopathy is objectively differentiated from the orotic acid-induced hepatopathy and the D-galactosamine-induced hepatopathy of inhibiting the onset of orotic. Applicant further argues that even though some ingredient is known to have an activity acid-induced hepatopathy or D-galactosamine-induced hepatopathy or an activity of healing it, it can never be expected easily whether or not the very ingredient has also an activity of inhibiting the alcoholic hepatopathy or an activity of healing it. Applicant further argues that the effects achieved by the presently claimed composition are unexpected over the prior art.

However, this is not found persuasive because Omori teaches a composition having a fatty liver suppressing activity fractionated from residual liquid of barley *shochu* liquor distillation comprising of an unadsorbed fraction obtained by subjecting barley *shochu* stillage by-produced in the production of barley *shochu* to solid-liquid separation and filtering the material to provide a liquid fraction, wherein the fraction as taught by Omori, is obtained in the same way and produced in the same manner as the composition and fraction claimed by Applicant and is one and the same as the composition and fraction claimed by Applicant. Therefore, the peptide length, amount of amino acids in the peptides, amount of amino acids derived from the peptides and the amount of saccharides, polysaccharides and organic acids in the composition taught by Omori are the same as that claimed by Applicant because these components are inherent to the composition taught by Omori and claimed by Applicant, absent evidence to the contrary.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the percent composition and that the composition according to the present invention contains the following elements: Organic Acid 2-8%, Polysaccharide 15-25%, Free Amino Acid 4-12%, Free Sugar 5-10% and that the fraction taught by Omori describes a composition comprising an ethanol-insoluble fraction containing an organic acid, protein and hemicellulose and formed by subjecting a barley shochu stillage to solid-liquid separation to obtain a liquid fraction, adding an alkali to the liquid fraction to collect with ethanol to accelerate synthesis of fatty acid or neutral fat in the liver,

inhibiting decomposition of fatty acid in the liver and the like is allegedly different than the composition claimed by Applicant, however, the teachings of Omori are one and the same as composition claimed, as written, by Applicant) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to Applicant's argument that as set forth in further detail in Applicants' specification, one of ordinary skill in the art would not have expected the unexpected effects produced by a composition according to the present invention, that is that the inhibition of the onset of alcoholic liver injury is unexpected based on the known activity of inhibiting the onset of orotic acid-induced hepatopathy disclosed by Omori or based on the known activity of inhibiting the onset of D-galactosamine-induced hepatopathy disclosed by other publicly known documents, that the alcoholic hepatitis is known to be hepatitis which is induced such that acetaldehyde or acetic acid, a metabolite of ethanol or active oxygen generated in producing the same damages hepatocytes, that the alcoholic hyperlipemia is known to be triggered such that excess neutral fat accumulated in the liver is released to blood in large quantities as a secretory very low density lipoprotein (VLDL), that such an alcoholic hepatopathy, it is known that lesion of hepatitis, such as balloon-like swelling or necrosis of hepatocytes, or a fatty liver comprising hepatocytes containing large fatty drops is progressed mainly on the terminal hepatic vein peripheral region of the hepatic lobule, that the liver is an assembly of a large number of the hepatic lobules each having a diameter of 1 mm in

which the hepatic lobule partitioned by an interlobular connective tissue functions as one unit, that accordingly, in view of the causative sequence of such hepatopathies, the alcoholic hepatopathy is objectively differentiated from the orotic acid-induced hepatopathy and the D-galactosamine-induced hepatopathy of inhibiting the onset of orotic, that even though some ingredient is known to have an activity acid-induced hepatopathy or D-galactosamine-induced hepatopathy or an activity of healing it, it can never be expected easily whether or not the very ingredient has also an activity of inhibiting the alcoholic hepatopathy or an activity of healing it, it is unclear as to what Applicant is arguing. It appears that Applicant is trying to further describe what Applicant means by alcoholic hepatopathy, however, please note that alcoholic hepatopathy is defined as disease of the liver caused by alcohol and refers to any disease of the liver. Therefore, alcoholic fatty liver disease is one type of alcoholic hepatopathy and, consequently, Omori teaches the instantly claimed invention.

Applicant's arguments, see "Applicant Arguments/Remarks Made in an Amendment", filed 31 October 2006, with respect to the rejection(s) of claim(s) 1-4 under 35 U.S.C. 102(b) as being anticipated by Yamamoto (O*) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn.

Claim Rejections - 35 USC § 103

Claims 1-7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Omori et al. (N*), in view of Kaneuchi et al. (P*).

The teachings of Omori are set forth above and applied as before.

Kaneuchi teaches a bowl movement improver, which reads on composition, comprising of a protein fraction derived from beer lees (please note that beer is made from three types of barley and undergoes a fermentation process like shochu production), wherein the beer lees is milled (in a wet state), sieved, further milled, further sieved and dried by freeze-drying or warm air dessication (See abstract and paragraph 0013). Kaneuchi further teaches a protein fraction containing glutamic acid in an amount of between 1 and 40%, wherein a specific example taught by Kaneuchi teaches glutamic acid in an amount of 22.5%. Kaneuchi further teaches glycine in an amount of 3.66%, proline in an amount of 10.64% and serine in an amount of 4.49% (See paragraph 0028). Kaneuchi further teaches the protein fraction from beer lees further contains saccharides (See paragraph 0011). Kaneuchi further teaches that the protein fraction may be used as a drug (See paragraphs 0019-0021).

The teachings of Omori and Kaneuchi are set forth and applied as before. Omori does not expressly teach that the composition comprising of an unadsorbed fraction which is formed by subjecting a barley shochu stillage byproduced in the production of shochu from a barley as a raw material to solid-liquid separation to obtain a liquid fraction and subjecting the liquid fraction to a separation treatment by adsorption using a synthetic adsorbent is a freeze-dried powder, nor does Omori teach a composition used as a drug, nor does Omori teach the synthetic adsorbant is an aromatic synthetic adsorbant or a methacrylic synthetic adsorbant. However, at the time the invention was made, it would have been obvious to one of ordinary skill in the art and one would have

been motivated and had a reasonable expectation of success to modify the composition taught by Omori to provide the instantly claimed invention by freeze-drying the composition comprising of an unadsorbed fraction from barley *shochu* stillage, to use the composition comprising of an unadsorbed fraction from barley *shochu* stillage as a drug and to use an aromatic synthetic adsorbant or a methacrylic synthetic adsorbant because at the time the invention was made it was well known in the art that a protein fraction obtained from alcohol fermentation comprising of a high percentage of glutamic acid and comprising of other amino acids was freeze dried and was used as a drug, as clearly taught by Kaneuchi. Moreover, it would have been merely a matter of judicious selection to one of ordinary skill in the art at the time the invention was made to modify the form in which the unadsorbed fraction is obtained and to choose what type of adsorbant to use to effectively filter the composition to obtain the desired purity of product. Thus, the claimed invention is no more than the routine optimization of a result effect variable.

The result-effective adjustment of particular conventional working conditions (e.g., adjusting the type of adsorbant material to use to filter a composition and what form a composition is in) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Based upon the beneficial teachings of the cited references, the skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

This rejection is maintained for reasons of record set forth in the paper mailed on 31 May 2006 and repeated below, slightly altered to take into consideration Applicant's amendment filed on 31 October 2006.

Applicant's arguments have been thoroughly considered, but the rejection remains the same for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant argues that the teachings of Omori are discussed above and that the disclosures of Kaneuchi et al do not overcome the deficiencies in Omori discussed above. Applicant further argues that Kaneuchi teaches a fraction derived from beer lees, where the wet beer lees is compressed into flakes and milled, followed by sieving treatment in the presence of water and the production process disclosed by Kaneuchi does not include "koji-production", "distillation", or "a separation treatment by adsorption using a synthetic adsorbent". Applicant further argues that koji-production is a biological manipulation in which a diastatic enzyme produced by koji-kin saccharizes the starch and since koji-kin produces not only amylase but also a wide variety of protease and peptidase, protein is subjected to various modifications (e.g. deoligomerization) during the process of koji-production. Applicant further argues that in the distillation process, heating treatment causes various reactions such as association and dissociation of protein, and, therefore, the degrees of polymerization and coupling of beer lees, not

subjected to a koji-production process and a distillation process, differ from those of the residual liquid of distilled spirit, subjected to these processes, even if they contain similar amino acids that constitutes the protein and peptides. Applicant further argues that these compositions are different and have disparate characteristics that are completely different from each other (See also Table 7 and Table 8 of the present application). Applicant further argues that there is some overlap between the glutamic acid content of the present invention and that described by Kaneuchi (JP8-157385), however, the content of amino acid such as glycine and serine disclosed by Kaneuchi does not fall within the range of the embodiments of the subject application. Applicant further argues that the content described in Kaneuchi: 3.66 percent by weight of glycine, 4.49 percent by weight of serine and the content described in the subject application: 4 to 20 percent by weight of glycine, 4 to 8 percent by weight of serine. Applicant further argues that the above difference additionally shows that these compositions are completely different from each other. Applicant further argues that as described in paragraphs [0017] and [0018] of Kaneuchi, the fraction is further concentrated using a protein-extracting reagent, and the resulting concentrate is subjected to usual dialysis and ultra-filtration, followed by freeze-drying to obtain a protein fraction and that the resulting protein fraction is obtained as freeze-dried powder, not the freeze-dried powder of unadsorbed fraction that is discussed therein. Applicant further argues that furthermore, according to the present invention, protein having 10-40 percent of glutamine and glutamic acid with respect to the percent of constituent amino acid may be separated from the above fraction derived from beer lees and that the amino acid

composition of the protein obtained in that manner was almost the same as the amino acid composition of the fraction derived from beer. Applicant further argues that for example, the above fraction derived from beer lees/husk is heated to reflux for a few hours with the extracting reagent described in the next paragraph. Applicant further argues that the mixture is filtered to obtain a solution having a high protein concentration. Applicant further argues that a solution is subsequently subjected to dialysis, and ultra-filtration, etc., in an ordinary manner. Applicant further argues that, finally, a protein fraction is obtained by a freeze-drying method, etc. and that the protein fraction may be purified by an ammonium sulfate precipitation method. Applicant further argues that the composition of the protein extraction reagent: Thirty gram of sodium lauryl sulfate, 18.6 g of EDTA disodium salt, 6.18 g of NaaB407, 4.56 g of NaHPO4, and 10 ml of ethylene glycol monoethyl ether were determined using 1 L of distilled water to adjust the pH of the solution to 6.9 to 7.1. Applicant further argues that one hundred milliliter of the resulting solution is added per one gram of a sample. Applicant further argues that the aforementioned unadsorbed fragment has the form of freeze-dried powder, ... (text omitted) and for the above reasons, each of the cited references is quite different from Applicants' claimed invention. Applicant further argues that even if the cited references are combined, it is respectfully submitted that it would not have been obvious to one of ordinary skill in the art to select the inventive composition and it is respectfully submitted that the beneficial results achieved by the inventive composition would not have been expected to one skilled in the art.

However, this is not found persuasive because at the time the invention was

made, it would have been obvious to one of ordinary skill in the art and one would have been motivated and had a reasonable expectation of success to modify the composition taught by Omori to provide the instantly claimed invention by freeze-drying the composition comprising of an unadsorbed fraction from barley *shochu* stillage, to use the composition comprising of an unadsorbed fraction from barley *shochu* stillage as a drug and to use an aromatic synthetic adsorbant or a methacrylic synthetic adsorbant because at the time the invention was made it was well known in the art that a protein fraction obtained from alcohol fermentation comprising of a high percentage of glutamic acid and comprising of other amino acids was freeze dried and was used as a drug, as clearly taught by Kaneuchi. Moreover, it would have been merely a matter of judicious selection to one of ordinary skill in the art at the time the invention was made to modify the form in which the unadsorbed fraction is obtained and to choose what type of adsorbant to use to effectively filter the composition to obtain the desired purity of product. Thus, the claimed invention is no more than the routine optimization of a result effect variable.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., koji-production) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, Claim 1 constitutes a Product-by-Process type claims. In Product-by-Process type claims, the process of producing the product is given no patentable weight

since it does not impart novelty to a product when the product is taught by the prior art. See *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983) and *In re Brown*, 173 USPQ 685 (CCPA 1972). Consequently, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught in by the prior art. See *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 599, 601, 38 USPQ 143-145 (CCPA 1938); *In re Bergy*, 563 F.2d 1031, 1035, 195 USPQ 344, 348 (CCPA 1977) *vacated* 438 US 902 (1978); and *United States v. Ciba-Geigy Corp.*, 508 F. Supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979). Finally, since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Therefore, it does not matter how the fraction is made, what matters is that the fraction shares the same elements as the claimed fraction.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

No claims are allowed.

Conclusion

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy L. Clark whose telephone number is (571) 272-1310. The examiner can normally be reached on 8:30am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele C. Flood

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PRIMARY EXAMINER

Amy L. Clark
AU 1655

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January 19, 2007